

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. With this amendment, claim 22 has been amended, claims 39 and 40 have been cancelled without prejudice or disclaimer, and no claims have been added. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier. Thus, claims 1-17, 22-34, 36-38, and 41-45 remain pending in the application.

Claim Rejections - 35 USC § 112/New Matter

Claims 39-40 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for allegedly introducing new matter. Applicant respectfully traverses this rejection.

Claims 39-40 have been canceled. Thus, this rejection is moot.

Claim Rejections - 35 USC § 112

Claims 39-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant respectfully traverses this rejection.

Claims 39-40 have been canceled. Thus, this rejection is moot.

37 CFR 1.132 Declaration

On page 5 of the Office Action, the Examiner states that the Declaration by Dr. Xing Su referenced in the Response dated January 31, 2008 was not submitted. Attached herewith is a copy of the referenced declaration.

Claim Rejections - 35 USC § 103

Claims 1, 2, 5-7, 9, 10, 13-17, 37 and 38 were rejected under 35 U.S.C. 103(a) as being over Cao et al. (Science August 2005 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent Application No. 2003/0211488) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com).

Claims 3, 4 and 8 were rejected under 35 U.S.C. 103(a) as being over Cao et al. (Science August 2005 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent 6361944 March 26, 2002) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com) in view of Mirkin et al. (U.S. Patent No. 6,361,944) (referred to as Mirkin B).

Claim 11 was rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al. (Science August 2002 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent Application No. 2003/0211488) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com) and in view of Pastinen et al. (Genome Research July 2000 Vol. 10(7) p. 1031).

Claim 12 was rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al (Science August 2002 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent Application No. 2003/0211488) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com) and in view of Lane et al. (US Patent 5,770,365 June 23, 1998).

Claims 22-24, 26-27, and 29-32 were rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al (Science August 2002 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent Application No. 2003/0211488) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com) and in view of Chan et al. (US Patent Application Publication) and Corbierre et al. (Journal of American Chem. Soc 2001 Vol. 123 p. 10411).

Claim 25 was being rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al (Science August 2002 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent Application No. 2003/0211488) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com) and in view of Chan et al. (US Patent Application Publication) and further in view of Bruchez, Jr. et al. (US Patent Application 09/815585).

Claim 28 was rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al (Science August 2002 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent Application No. 2003/0211488) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com) and in view of Chan et al. (US Patent Application Publication) and further in view of Livak et al. (US Patent 5,723,591).

Claims 33, 39, and 43 were rejected under 35 U.S.C. 103(a) as being over Cao et al (Science August 2002 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent Application No. 2003/0211488) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com) and in view of Garimella et al. (US Patent Application Publication 2003/0082588).

Claims 34, 36, and 40 were rejected under under 35 U.S.C. 103(a) as being over Cao et al (Science August 2002 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent Application No. 2003/0211488) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com) and in view of Garimella et al. (US Patent Application Publication 2003/0082588) and further in view of Mirkin et al. (US Patent 6361944).

Claims 41-42 and 44 were rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al (Science August 2002 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent Application No. 2003/0211488) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com) and in view of Garimella et al.

(US Patent Application Publication 2003/0082588) and in view of Corbierre et al. (Journal of American Chem. Soc 2001 Vol. 123 p. 10411).

Claim 45 was being rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al (Science August 2002 Vol 297 p. 1536) as evidenced by Faulds et al. (Talanta 2005 vol. 67 p. 667) in view of Mirkin et al. (US Patent Application No. 2003/0211488) as evidenced by Glen Research Catalog (Catalog Number 105913 www.glenresearch.com) and further in view of Vo-Dinh (US Patent 5,721,102).

Applicants respectfully traverses the rejections.

The asserted combinations of Cao et al., Faulds et al., Mirkin et al., Glen Research Catalog, Mirkin B, Pastinen et al., Lane et al., Chan et al, Bruchez, Jr. et al., Livak et al., Garimella et al., Vo-Dinh, and Corbierre et al. would not have rendered claims 1-17, 22-34, 36-38, and 41-45 obvious to one of ordinary skill at the time of invention because none of the references singly or in combination teach or suggest all of the recited features of independent claim 1, 22, and 33. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). *See also* MPEP 2143.03.

Independent claim 22 has been amended to recite “wherein the labeled oligonucleotide probe comprises a positively charged Raman signal enhancer, ***the positively charged Raman signal enhancer maintaining its positive charge after binding with the probe-target complex.***”

Independent claims 1 and 33 include the feature “***the positively charged Raman signal enhancer maintaining its positive charge after binding with the probe-target complex.***” As illustrated in the figure in the Su declaration attached herewith, the claimed nucleic acid-tag complex is not attached to a metal particle and therefore maintains its charge. Further, as taught in the present specification,

Oligonucleotides that do not intrinsically generate a Raman signal, or that generate a weak Raman signal, in some aspects, are covalently bound to a positively charged enhancer. Accordingly, disclosed herein are populations of oligonucleotides, at least some of which are covalently attached to a positively

charged enhancer. As illustrated in the Examples herein, for example, oligonucleotides with a high percentage of pyrimidine nucleotides can have weak or undetectable intrinsic Raman activity. These oligonucleotides can be covalently bound to a positively charged group to render the Raman signal detectable or to increase the intrinsic signal generated by the oligonucleotide, as illustrated in the Examples herein. Not to be limited by theory, it is believed that the positively charged groups increases the association and orientation of the oligonucleotide with a SERS surface. Alternatively, a pyrimidine-rich oligo nucleotide can be hybridized, completely or partially, to an adenosine-rich oligonucleotides to obtain an enhanced Raman signal. (Paragraph [0022]).

That is, the positively charged enhancer allows detection of oligonucleotides that do not intrinsically generate a Raman signal. In the office action, the Examiner states “Cao et al. teaches the positively charged enhancer but does not indicate the method of making the enhancer so it is not clear from the teachings if the positive charge is present after binding with the probe-target complex.” (Office action, p.8, ¶6, 1.13-15). The Examiner then states “Mirkin et al. teaches that the oligonucleotide is attached to the phosphoramidite and the linker is attached to the DMT (displayed as MMTO on the figure) (p. 10 paragraph 158). Therefore the positively charged amine is not effected by the attachment of the linker and the oligonucleotide and would maintain its positive charge after binding to with the probe-target complex.” (Office action, p.9, 1.1-5). The Examiner, however, is incorrect. As discussed in paragraph (5) of the Su declaration, “When the charged Cy3 labeled oligonucleotide of Cao et al. is attached to the gold particle, the Cy3 **label** loses its positive charge.” The fact that the linker is attached to the DMT is irrelevant. *All charge carried by the Cy3 label is lost upon bonding to the gold particle.* This fact is irrefutable that persons of ordinary skill in this art would recognize, and Dr. Su has made a sworn statement to this effect in his declaration. If the Examiner still thinks that Dr. Su’s sworn statement is incorrect based on some personal knowledge, then the Examiner is respectfully requested to submit a sworn statement to this effect or provide evidence to support the Examiner’s position. Thus, the combination of Cao et al. Mirken does not teach or suggest methods “wherein the positively charged Raman signal enhancer maintain[s] its positive charge after binding with the nucleic acid.” Further, the Examiner has not indicated how any of the other cited references teach or suggest this feature. Applicant, therefore respectfully requests withdrawal of the rejections.

Double Patenting

Claims 1, 4 and 43 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 11/414,681. Claims 1, 4 and 43 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application no. 11/414,611.

Because the claims of present application and the cited applications may be amended significantly during prosecution, Applicant respectfully requests these rejections be held in abeyance until the indication of allowable subject matter.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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